

Pharmaceutical Quality System (ICH Q10) Conference

*A Practical Approach to Effective Lifecycle Implementation
of Systems and Processes for Pharmaceutical Manufacturing*

October 4-6, 2011 | Crystal Gateway Marriott | Arlington, Virginia
November 14-16, 2011 | Sheraton | Brussels, Belgium

Welcome

Pharmaceutical Quality Systems (ICH Q10) Conference

Business Case for Quality

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The Cost of Non-Compliance

– Presentation Agenda

- Business Case
 - Why quality and compliance are critical (to the bottom line)
- Survey Findings
 - Pharmaceutical Manufacturing Research Program (PMRP) Survey
 - PDA in collaboration with ISPE has conducted a benchmarking survey to better understand the cost of poor quality systems. The results of this survey will be shared with participants at both conferences!

The Cost of Non-Compliance

– The (Internal) Costs

- Direct Costs
 - Related to Product Failure, Scrap, etc.
 - E.g., Raw Materials, Process, Operations, etc.
- “Continual Crises” Costs
 - Unexpected costs associated with QS / GMP noncompliance
 - Reactive (noncompliant) versus preventive (compliant) approaches
- Remediation Costs
 - Related to problem identification, correction and reporting

The Cost of Non-Compliance

– The (External) Costs

- Regulatory Action Costs
 - Related to Legal, 3rd Party, Disgorgement, etc.
 - Related to Recalls, Discontinuation, Suspended Operations, etc.
- Market Share Costs
 - Related to Volumes, Supply Availability/Reliability, etc.
- Reputational Costs
 - Related to product spillovers, corporate spillovers, shareholder value, etc.

What is the Cost of a Consent Decree?

Several Companies have Stated that the CD has cost more than \$2 Billion

1) Direct Cost	<ul style="list-style-type: none"> • Site Remediation • Increased Headcount • Improve all other Sites 	Cost that Company should have invested prior to Regulatory Action to maintain operations.
2) Business Cost	<ul style="list-style-type: none"> • Product Recall / Destruction • Production Discontinuation / Withdrawal • No New Approvals 	Variable \$100 Million plus
3) Third-Party Controls	<ul style="list-style-type: none"> • Investigation • Batch Record Reviews • Quality Unit Reviews • Management Control Reviews • Validation • Inspections & Audits • Certifications • Legal 	Up to \$100 Million
4) Penalties	<ul style="list-style-type: none"> • Disgorgements (return of profits) • Late Completions 	Up to \$500 Million Up to \$15K per day, per action
5) Product Value / Reputation	<ul style="list-style-type: none"> • Patients • Customers 	\$100 Million Some have lost all market share
6) Value / Goodwill	<ul style="list-style-type: none"> • Shareholders 	Billions Drastic loss of stock value
7) Litigation	<ul style="list-style-type: none"> • Civil, (e.g., Product Liability) • Criminal • Shareholder Derivative • False Claims Act 	Up to \$1 Billion

The Costs of Non-Compliance – The Benefits of Compliance

- Improved Process Efficiency
 - Related to higher yield, lower cycle time, lower failures, etc.
- Lower Investigations / Risks
 - Related to deviations, rejects, OOS, etc.
- Increased Customer Satisfaction
 - Related to lower returns, lower complaints, etc.
 - Which translate to reputation, market share, etc.
- Superior Return on Investment (ROI)

The Cost of Non-Compliance

– PMRP Survey

- Goal
 - To identify factors that contribute to manufacturing and deviation performance of pharmaceutical manufacturing
- Participants
 - 19 unique pharmaceutical firms
 - 37 unique manufacturing facilities
 - 15 Active Pharmaceutical Ingredient (API) facilities
 - 22 Oral, Topical and Injectable (OTI) facilities
 - Over 150 compounds

The Cost of Non-Compliance

– PMRP Factors and Performance Metrics

Factors

- Managerial
 - Training, supervision and review of employees
 - Locus of decision rights (for problem solving)
- Organizational
 - Type and complexity of facility
 - Locus of reporting and decision rights
- Technical
 - Extent and use of IT, etc.

Performance Metrics

- Manufacturing
 - Batches Failed
 - Yield (Theoretical / Actual)
 - Cycle Time
- Deviation
 - Availability
 - Deviations Number and Type

The Cost of Non-Compliance

– PMRP Summary of Results

FACILITY FACTOR	OTI Manufacturing Performance Effect	API Manufacturing Performance Effect
MANAGERIAL – Employee Training – Lower Level Decision Rights – Multiple Review and Approval	Increase Increase	Increase
ORGANIZATIONAL – Complexity – Contract Manufacturer	Decrease Decrease	Increase Decrease
TECHNICAL – Extent and Use of IT	Increase	Increase

The Cost of Non-Compliance

– PMRP Summary of Results

FACILITY FACTOR	OTI Deviation Performance Effect	API Deviation Performance Effect
MANAGERIAL – Employee Training – Lower Level Decision Rights – Multiple Review and Approval	Mixed Decrease	Decrease
ORGANIZATIONAL – Complexity – Contract Manufacturer	Mixed	Increase Mixed
TECHNICAL – Extent and Use of IT	Decrease	Decrease

The Cost of Non-Compliance

– PMRP Conclusions

- **Management Choices Matter**

- Employee training impacts performance

- Create programs to improve quality education at all worker levels

- Locus of decision rights impacts performance

- Create processes that facilitate quality risk/improvement problem solving efforts at lower levels

- Multiple review and approval impacts performance

- Implement “team-based approaches” toward quality management

- **Quality Assurance is Critical**

- Contract manufacturers often have worse performance

- Create processes that select and qualify “right” CMs

The Cost of Non-Compliance

– PMRP Conclusions

- **Organization is Important**
 - Facility complexity has complex performance relationship
 - Consider “sensible” approaches to multi-product and multi-process facilities.
- **Technology is (an Increasing) Imperative**
 - Extent and use of IT associated with higher performance
 - Implement tools to collect, calculate and report on quality

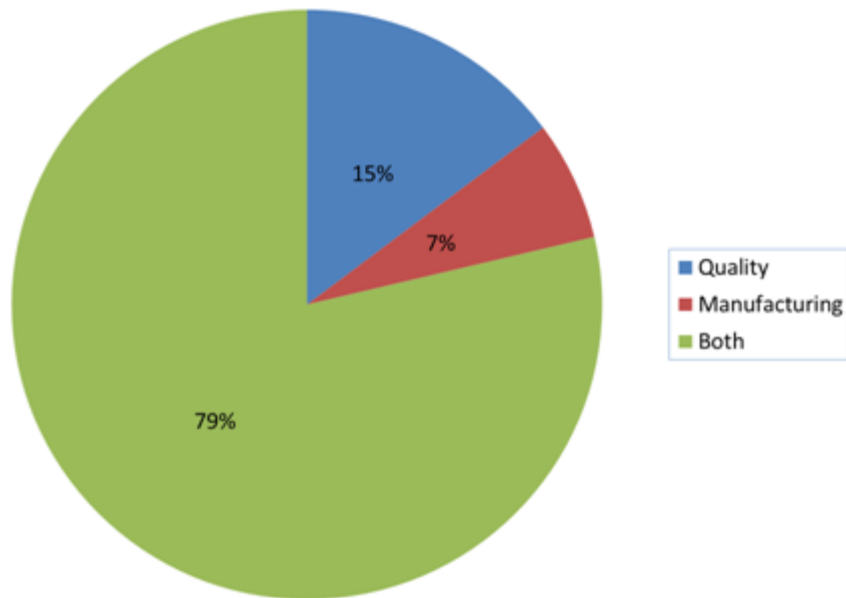
The Cost of Non-Compliance

-PDA/ISPE Business Case for Pharmaceutical Quality Survey

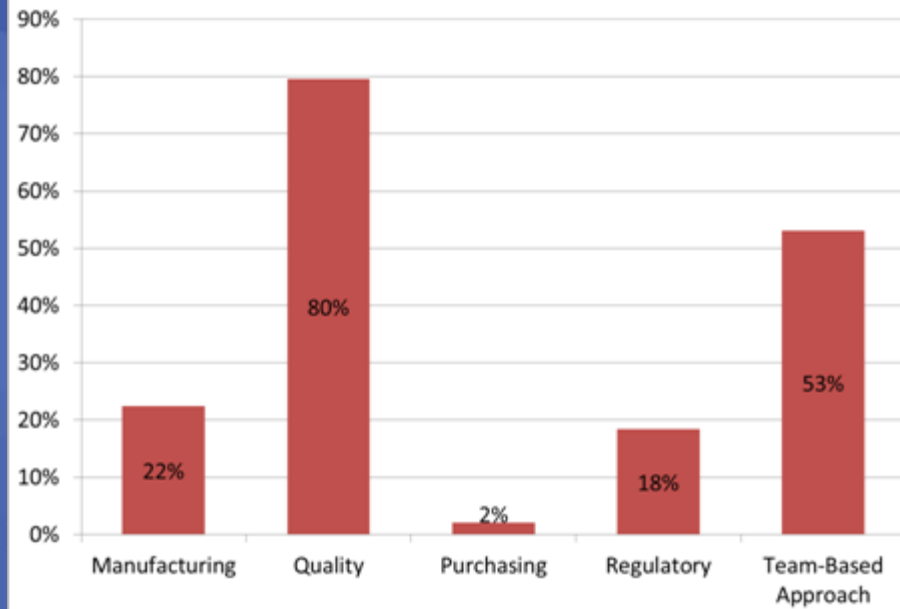
- Goal
 - To better understand the costs of poor quality and benefits of good quality systems in pharmaceutical manufacturing
- Participants
 - 62 respondents as of 14 SEP 2011.
 - Facilities
 - Innovators (67%), Generics (15%) & CMOs (18%)
 - United States (44%), Europe (27%) & Other (29%)
 - Products
 - Sterile Finished (31%), Non-Sterile Finished (44%), API (19%) & Other (7%)
 - Rx (51%) & OTC (49%)

The Cost of Non-Compliance – PDA/ISPE Summary of Results

Who is responsible for quality issues on the manufacturing floor?

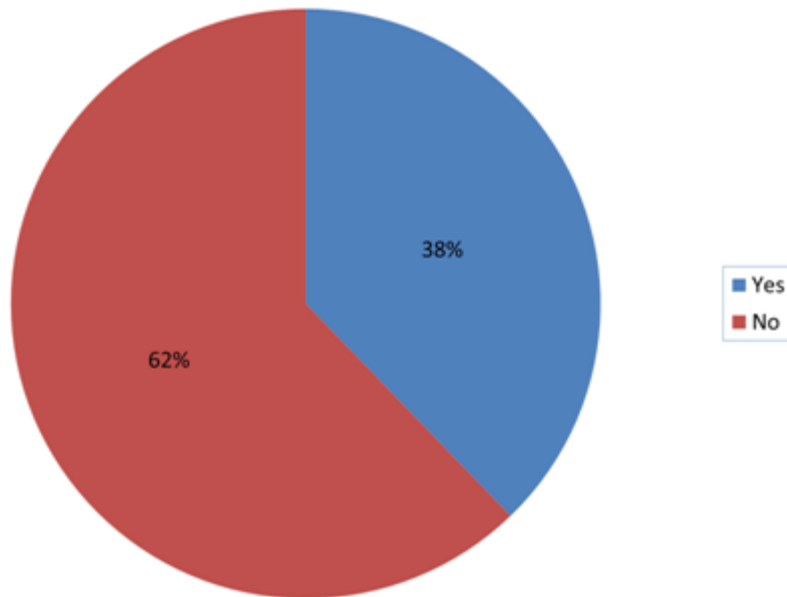


Who makes product quality risk decisions (check all that apply)?

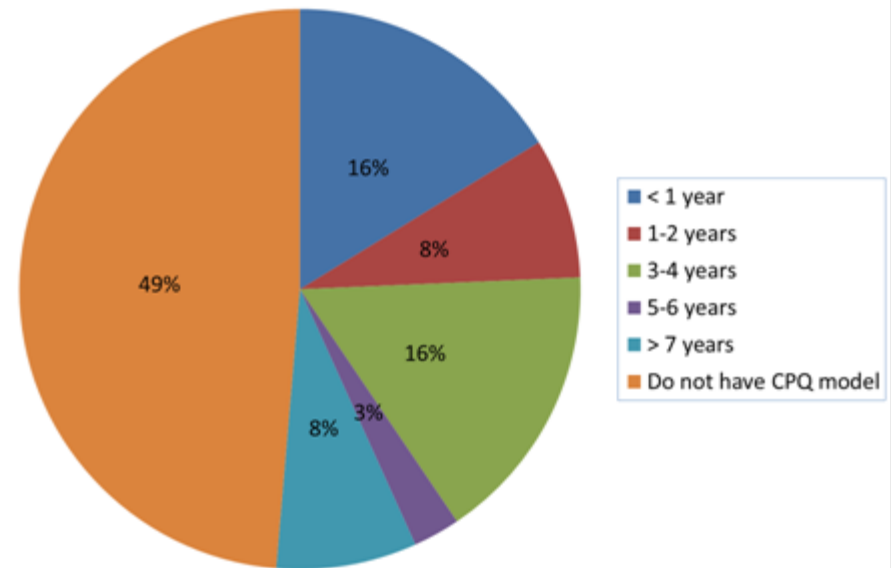


The Cost of Non-Compliance – PDA/ISPE Summary of Results

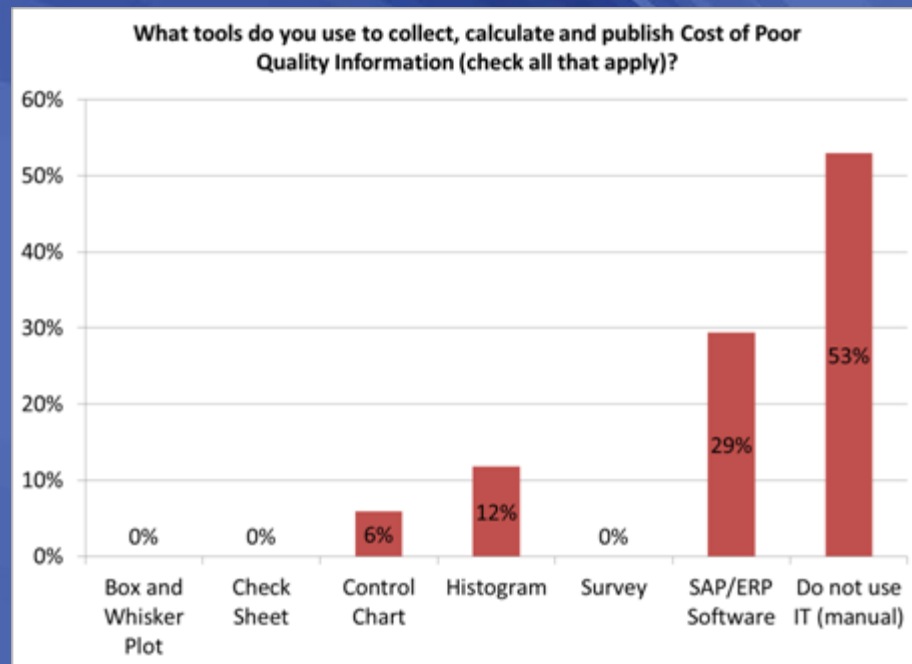
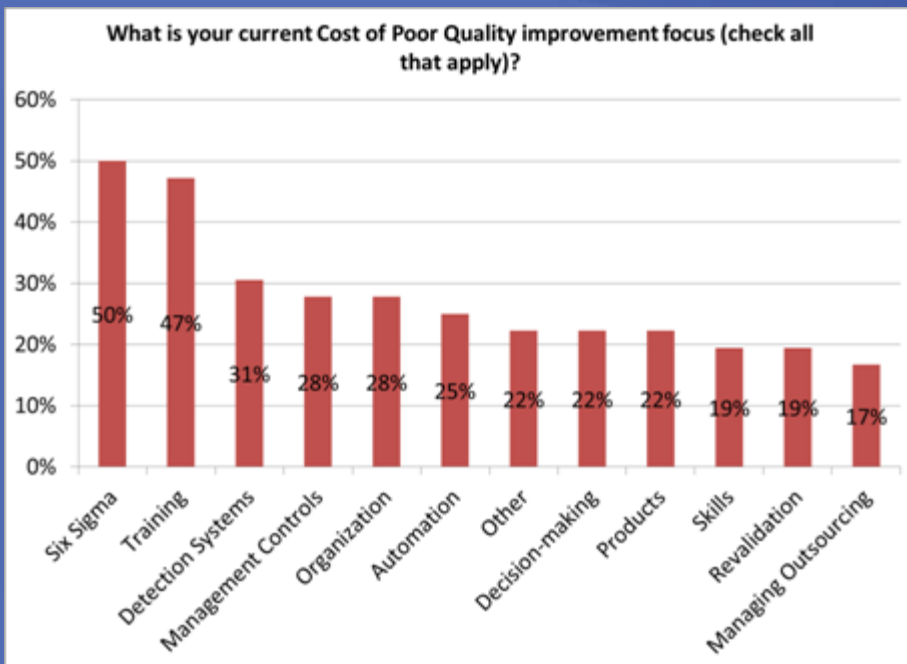
Do you calculate a Cost of Poor Quality at your site?



How long have you had a Cost of Poor Quality measurement Model and Process in Place?

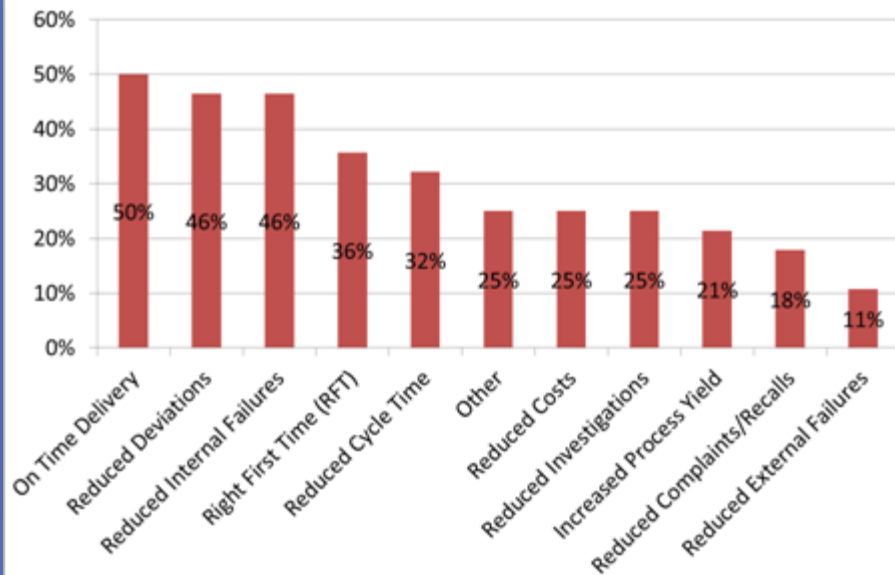


The Cost of Non-Compliance – PDA/ISPE Summary of Results

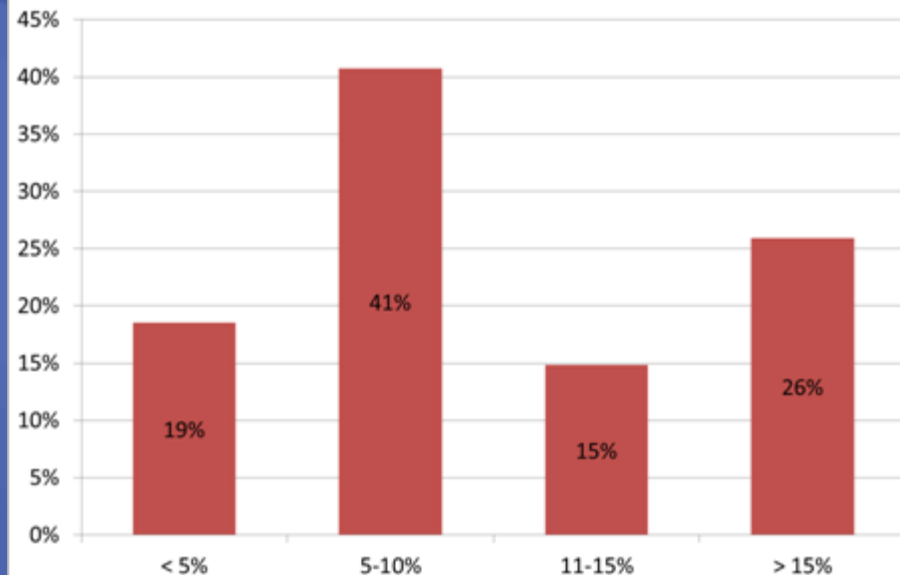


The Cost of Non-Compliance – PDA/ISPE Summary of Results

What significant benefits have you achieved through the measurement of Cost of Poor Quality (check all that apply)?

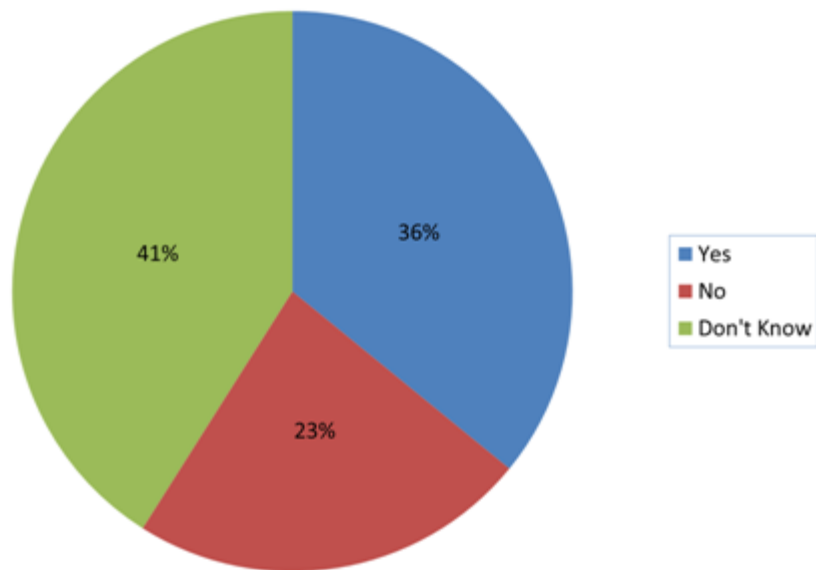


What percentage reduction are you targeting to set Cost of Quality improvement?

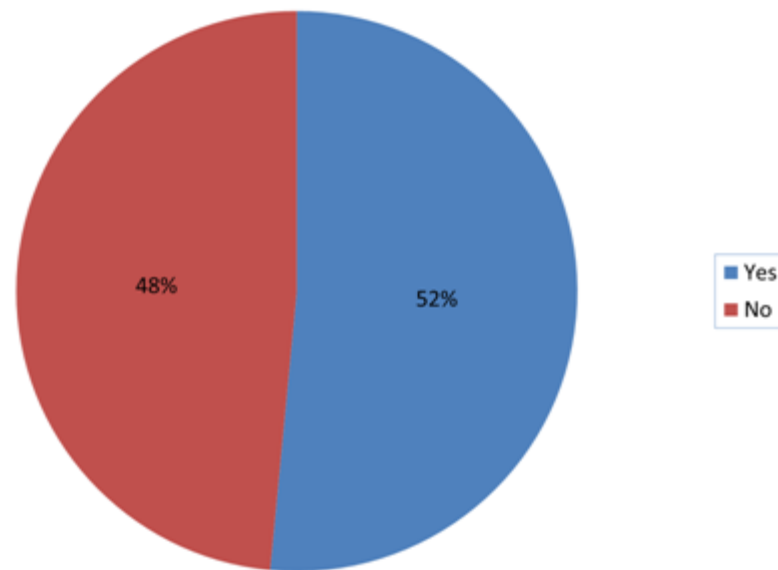


The Cost of Non-Compliance – PDA/ISPE Summary of Results

Have you observed (or are you expecting to observe) cost savings (direct or indirect) as a result of implementing elements of Q8, Q9 or Q10?

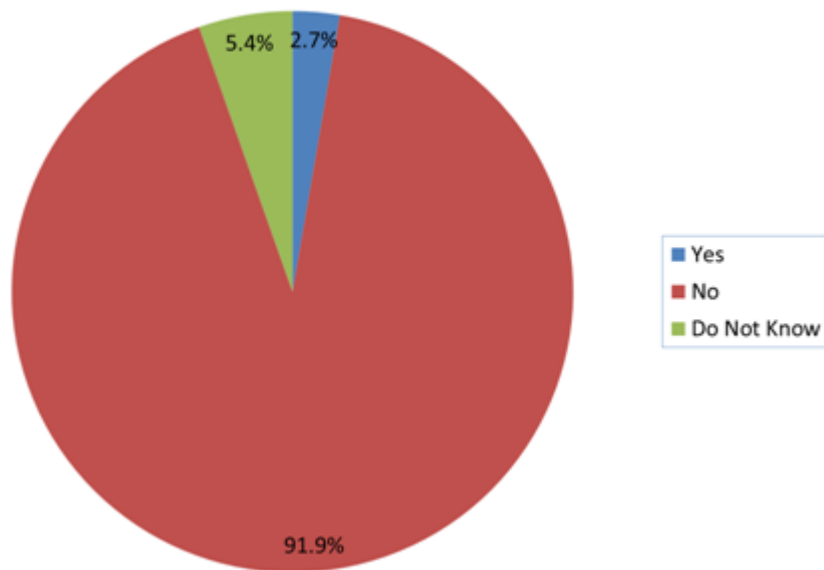


Has your company seen a reduction in deviation and investigation rate as a consequence of implementing ICH Q8-Q10?

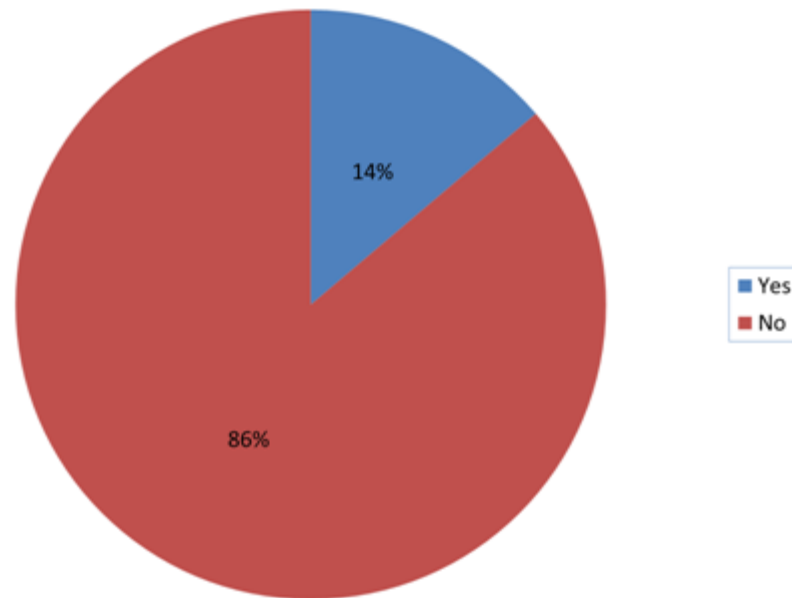


The Cost of Non-Compliance – PDA/ISPE Summary of Results

Have you evaluated the cost of improving quality vs. the cost of failure (recalls, rejections, low yield, downtime, etc.)?

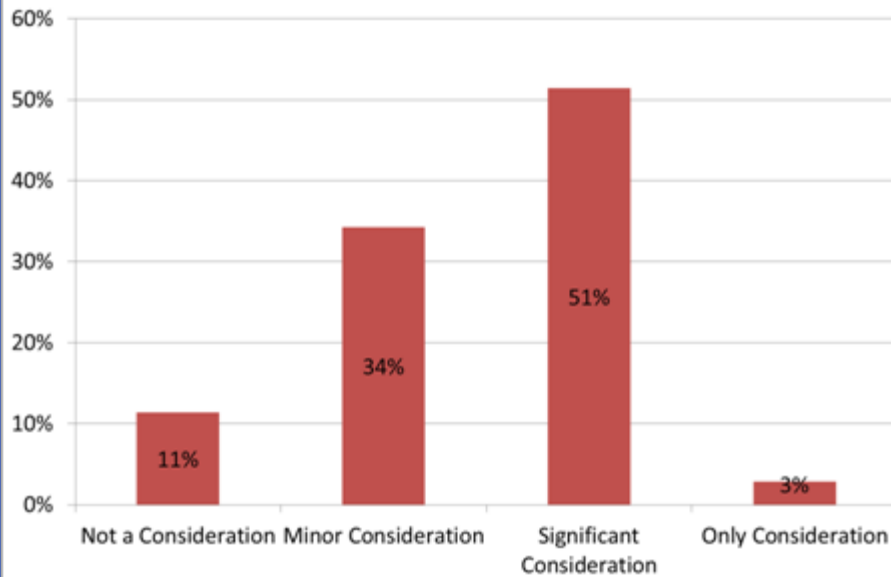


Have you conducted an ROI on your PAT?

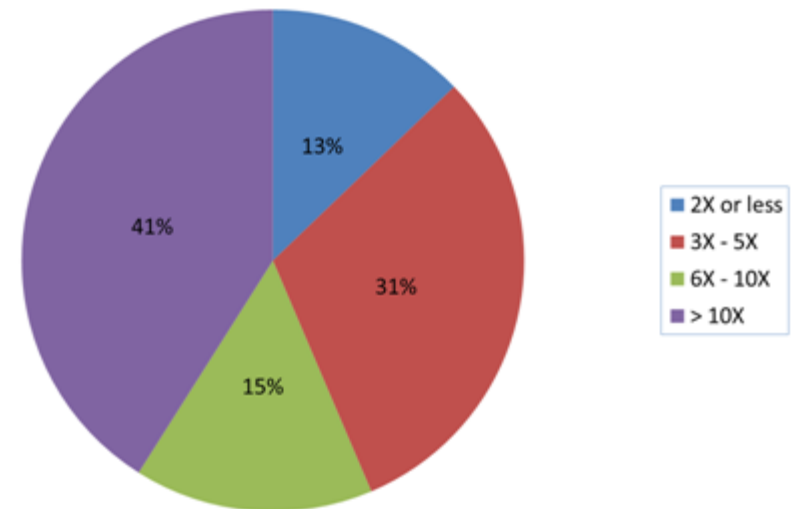


The Cost of Non-Compliance – PDA/ISPE Summary of Results

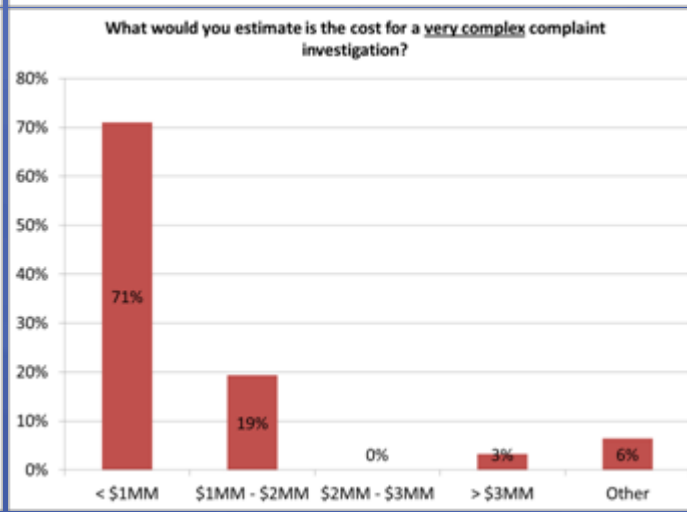
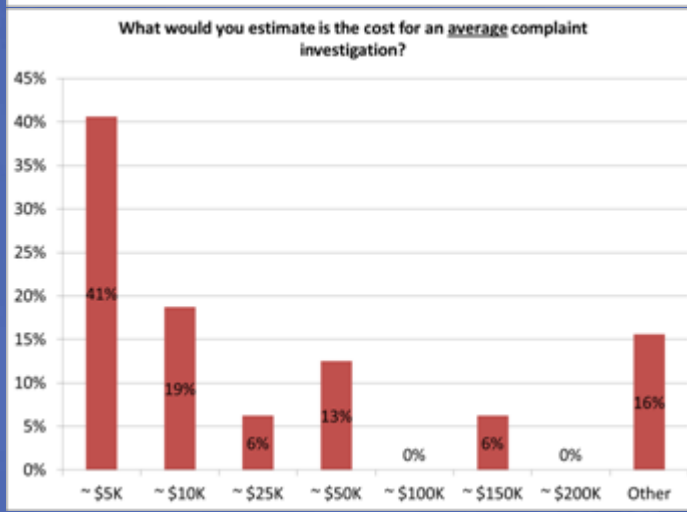
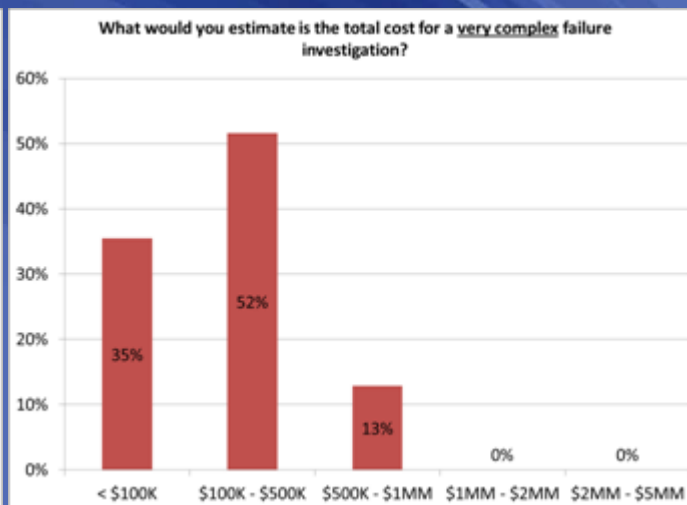
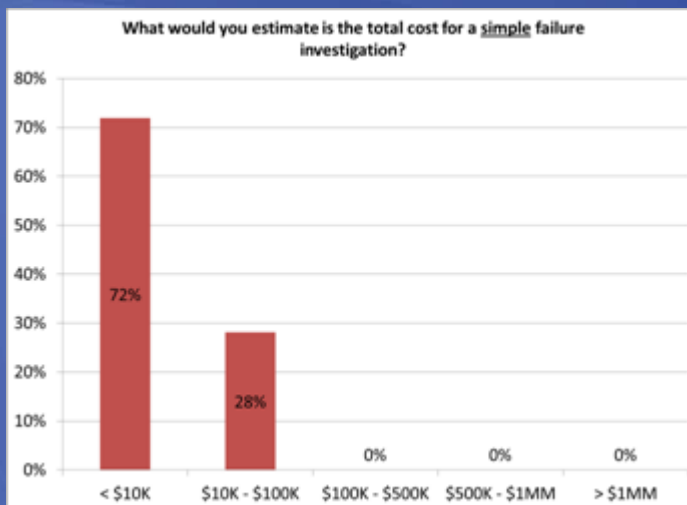
How much does cost weigh into decisions whether or not to fix problem areas?



On average, how much greater do you believe the cost is to correct a critical observation received from a Health Authority (in a reactive mode) when compared to early and proactive correction of the same critical observation?



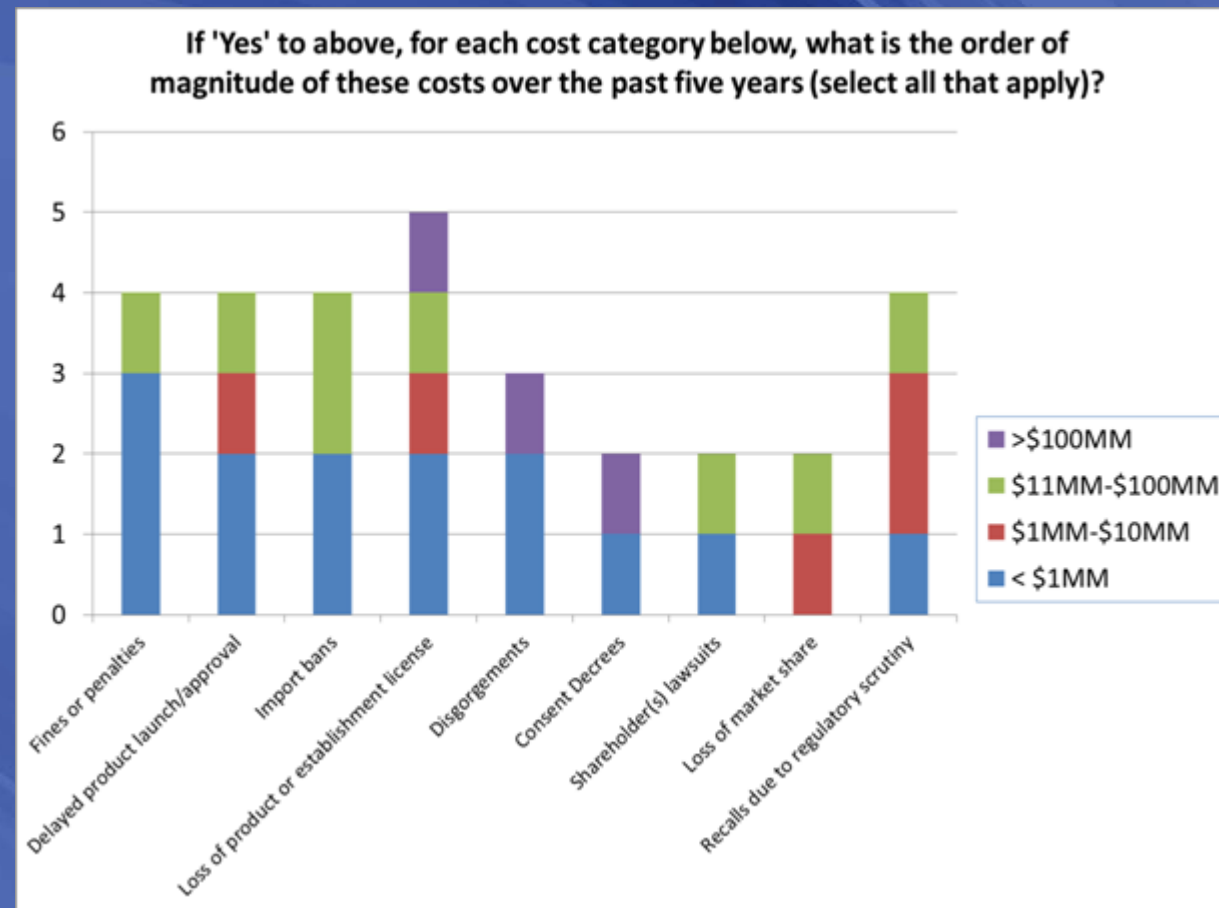
The Cost of Non-Compliance – PDA/ISPE Summary of Results



The Cost of Non-Compliance

– PDA/ISPE Summary of Results

- Have you incurred regulatory health authority sanction costs due to manufacturing deficiencies?
 - Yes – 12%
 - No – 88%



The Cost of Non-Compliance

–Conclusions

- **Substantial respondent heterogeneity exists**
 - Managerial and organizational approaches toward quality and compliance
 - Quality and compliance emphasis, objectives and performance
 - Reported costs of compliance
- **Many “other factors” increase compliance costs**
 - Reactive versus proactive approaches
 - Complex versus simple investigations

The Cost of Non-Compliance –Conclusions

- **Some questions and uncertainties remain**
 - Benefits of Cost of Poor Quality calculation
 - Placing a value on CoPQ?
 - Determining what functions to measure?
 - Gaining agreement on resources and focus?
 - Benefits of ICH Q8-10 implementation

The Cost of Non-Compliance –Survey Acknowledgements

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